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Comparison of Carisoprodol, Butabarbital, and Placebo in Treatment of the Low Back Syndrome

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■ *A double-blind study was carried out to determine the effectiveness of a muscle relaxant, carisoprodol, in the treatment of the low back syndrome, and to test whether this drug would produce any greater effect than an active sedative control. Forty-eight Mexican migrant farm laborers with acute lumbar strain and spasm were given either carisoprodol 350 mg, butabarbital 15 mg, or placebo, four times daily for four days, and then were rated on pertinent symptoms, the degree of limitation of motion (by an objective finger-to-floor test), and overall improvement. In the 43 patients who could be statistically analyzed, carisoprodol was shown to be significantly more effective than butabarbital or placebo in producing improvement of all factors rated. This result suggests that the effects of carisoprodol are not due solely to sedative action, but are also related to its muscle relaxant activity.*

THE ADJUNCTIVE USE OF MUSCLE RELAXANT drugs in the management of pain, spasm, and stiffness associated with musculoskeletal trauma has found wide support in clinical practice.[1-5] Notwithstanding this fact, the effectiveness of these agents, when given orally, has been questioned, and their benefits sometimes attributed simply to their sedative action.[6-7]

Since our practice serves a large number of migrant farm laborers whose work frequently produces acute lumbar strain, it appeared to offer a suitable clinical situation for conducing a controlled test of a muscle-relaxant drug.

The Study

A double-blind study was undertaken to evaluate the efficacy of carisoprodol Soma® in relieving pain and spasm in the "low back syndrome." Placebo was used as an inactive control and butabarbital 15 mg as an active sedative control. A higher dosage of butabarbital was not used because the resultant drowsiness might have broken the "blindness" of the study.

The Population

The subjects of this study were all Mexican braceros, contract laborers who cross the border into California to farm the crops of the Imperial Valley. Because of protracted stooping and carrying, the "low back syndrome," characterized by lumbar spasm and acute lumbar strain, is an occupational hazard in this population. Forty-eight patients with this condition entered the trial. Twenty-seven were men and 21 women, with ages ranging from 18 to 70 years (average 38.4). In 37 patients the onset of symptoms had occurred within the preceding 12 to 24 hours; in

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TABLE 1.—*Time from Onset of Symptoms to Baseline Evaluation*

Time (Hours)	*Carisoprodol (N=16)*	*Butabarbital (N=16)*	*Placebo (N=16)*
0-12	1	3	2
12-24	14	11	12
24-48	1	2	2

TABLE 2.—*Demographic Distribution*

	Carisoprodol (N=16)		*Butabarbital (N=16)*		*Placebo (N=16)*		*All Treatments (N=48)*	
	M	*F*	*M*	*F*	*M*	*F*	*M*	*F*
Age								
Under 20	—	—	—	2	—	—	—	2
20-30	4	3	2	2	2	1	8	6
31-40	2	2	5	1	3	3	10	6
41-50	1	1	—	3	1	2	2	6
51-60	1	—	1	—	1	—	3	—
61-70	1	1	—	—	3	—	4	1
Total	9	7	8	8	10	6	27	21
Average	37.0		34.6		43.5		38.4	
Median	35.0		36.0		38.0		37.0	
Range	21-66		18-52		24-70		18-70	

six cases, within less than 12 hours; and in five, within 24 to 48 hours of initial treatment (Table 1).

Method

Patients were assigned sequentially, as they entered the study, in accordance with an allocation schedule derived from a table of random numbers.[8] (After completion of the trial, it was made known to the investigator that randomization had been carried out in groups of six, two patients per drug, in order to balance the treatment groups over time.) This assignment put 16 patients, comparable as to age and sex, into each drug group (Table 2). Five patients dropped out at various stages of the trial (Table 3). The loss of these five patients left 14 in the carisoprodol and placebo groups and 15 in the butabarbital group who completed the study. These treatment groups remained comparable for age, sex, and time of symptom onset.

Medications were provided* as identically appearing tablets of carisoprodol 350 mg, butabarbital sodium 15 mg, or placebo, each patient receiving the medication coded for his roster number, in bottles labelled to keep either the

*By Wallace Pharmaceuticals, Cranbury, New Jersey.

TABLE 3.—*Reasons for Dropouts at Various Stages of Trial of Muscle Relaxant Drug*

Medication	*Patient No.*	*Age*	*Sex*	*Onset (Hours)*	*Reason for Discontinuance*
Carisoprodol	42	21	M	0-12	Condition worsened. Patient sought another doctor after day 2 for pain medication.
	43	66	F	12-24	Patient refused to continue in study after initial visit. No evaluation possible.
Butabarbital	25	43	F	12-24	Dropped from study because of drowsiness first day on drug. No evaluation possible.
Placebo	21	30	M	12-24	Not seen after first visit. No evaluation possible.
	48	38	M	12-24	Condition worsened. Patient refused to continue after day 2.

patient or the investigator from identifying the medication. The treatment in all cases consisted of one tablet of the assigned medication taken three times a day and at bedtime for four days. Specific medications for concomitant diseases were permitted, but these did not include sedatives, tranquilizers, or muscle relaxants. Patients remained off their jobs as long as pain continued.

Measurements and Rating Criteria

On first examination, and on days two and four after start of medication, the following ratings were recorded:

1. Evaluation by the investigator of the severity of the following symptoms: pain, spasm, interference with daily activities, limitation of motion, and anxiety and tension (if present). A four-step severity rating scale was used: 1=none, 2=mild, 3=moderate, 4=severe. An overall average severity score was also calculated for each patient by dividing the sum of the individual symptom severity scores by the number of symptoms at baseline.

2. Objective evaluation of the degree of limitation of motion by measurement of the distance (in centimeters) from fingertips to floor following maximal forward flexion (finger to floor test).

3. Patient estimation of the intensity of pain by placing a mark on a "pain intensity scale" representing a continuum between "no pain" (0 percent) and "unbearable pain" (100 percent).

TABLE 4.—*Average Symptom Scores and Significance of Differences at Baseline*

Parameter	Days on Drug	Average Scores			Baseline Differences	
		Carisoprodol (N=14)	Placebo (N=14)	Butabarbital (N=15)	Prob: Carisoprodol vs. Placebo	Butabarb.
Pain	Base	3.5	2.9	3.1	0.02	0.09
	2	2.4	3.0	2.9		
	4	2.1	2.9	2.6		
Spasm	Base	3.1	3.0	3.1	>0.25	>0.25
	2	2.4	2.9	2.8		
	4	1.8	2.9	2.6		
Interference with Daily Activities	Base	3.7	3.1	3.3	0.02	0.07
	2	2.4	3.1	2.9		
	4	1.8	3.4	2.7		
Limitation of Motion	Base	3.3	2.9	3.1	0.12	>0.25
	2	2.0	3.1	2.9		
	4	1.6	2.9	2.7		
Anxiety and Tension	Base	2.6	2.2[1]	2.4[2]	0.16	>0.25
	2	1.9	2.2[1]	2.2[2]		
	4	1.6	2.4[1]	2.2[2]		
Global Average Severity	Base	3.3	2.9	3.0	<0.01	0.04
	2	2.2	2.9	2.8		
	4	1.8	2.9	2.6		
Finger to Floor (cm)	Base	33.3	27.0	24.3	0.14	0.04
	2	17.6	27.6	22.0		
	4	13.7	25.7	18.9		
Patient Estimate of Pain Intensity (%)	Base	86.0	65.5	75.2	<0.01	0.01
	2	33.0	58.5	58.7		
	4	15.5	64.0	49.1		

[1]N=11 (3 placebo patients without anxiety and tension)
[2]N=12 (3 butabarbital patients without anxiety and tension)
Key:
Probability ≤0.05: significant difference between drug groups.
Probability >0.05 and ≤0.10: borderline significant difference between drug groups.
Probability >0.10: no significant difference between drug groups.

4. Final evaluation by the investigator of overall patient improvement. Global results were rated as:

Excellent=75 percent to complete relief of all symptoms with return to full activity.

Good=50-75 percent improvement in all symptoms with return to full activity.

Fair=25-50 percent improvement in all symptoms with some discomfort in doing daily activities.

Poor=Some improvement, but less than that described above.

Worse=Symptoms more severe than before entry into study.

Statistical Analysis

The Mann-Whitney U-Test was used to analyze the data of the carisoprodol as compared with the butabarbital group, and the carisoprodol against the placebo group, for each factor and for the overall evaluation.

Results

Symptomatic improvement: Table 4 shows the actual average symptom scores for each of the three test groups at baseline and at two and four days after the start of medication. Initial symptom severity scores are shown to have been higher for several factors in the carisoprodol group than in either of the other groups.

Table 5 shows the calculated improvement scores, and the statistical significance of differences between carisoprodol and placebo, and between carisoprodol and butabarbital. The analysis shows that:

1. Carisoprodol produced significantly greater relief of all symptoms—pain, spasm, interference with daily activities, limitation of motion, anxiety and tension ($P \leq 0.02$)—as well as greater overall average relief of these symptoms ($P < 0.01$) than placebo. Carisoprodol produced significantly greater objective improvement in the finger to floor test ($P = 0.01$), and greater reduction in

TABLE 5.—*Improvement of Measured Factors*

Parameter	Days on Drug	Average Improvement			Probability	
		Carisoprodol (N=14)	Placebo (N=14)	Butabarbital (N=15)	Carisoprodol vs. Placebo	Carisoprodol vs. Butabarbital
Pain	2	1.1	−0.1	0.2	<0.01	<0.01
	4	1.4	0.0	0.5	<0.01	0.01
Spasm	2	1.0	0.1	0.3	0.02	0.10
	4	1.3	0.1	0.5	0.01	0.02
Interference with Daily Activities	2	1.3	0.0	0.4	<0.01	0.01
	4	1.9	−0.3	0.6	<0.01	<0.01
Limitation of Motion	2	1.3	−0.2	0.2	<0.01	<0.01
	4	1.7	0.0	0.4	<0.01	<0.01
Anxiety and Tension	2	0.7	0.0[1]	0.2[2]	0.01	0.03
	4	1.0	−0.2[1]	0.2[2]	<0.01	0.04
Global Average Severity	2	1.1	0.0	0.2	<0.01	<0.01
	4	1.5	0.0	0.4	<0.01	<0.01
Finger to Floor (cm)	2	15.7	−0.6	2.3	<0.01	<0.01
	4	19.6	−1.3	5.4	0.01	0.02
Patient Estimate of Pain Intensity (%)	2	53.0	7.0	16.5	<0.01	<0.01
	4	70.5	1.5	26.1	<0.01	<0.01

[1]N=11 (3 placebo patients without anxiety and tension)
[2]N=12 (3 butabarbital patients without anxiety and tension)
Key:
Probability ≤0.05: significant difference between drugs
Probability >0.05 and ≤0.10: borderline significant difference between drugs
Probability >0.10: no significant difference between drugs

the intensity of pain experienced by the patient (P<0.01).

2. Carisoprodol also proved significantly more effective than butabarbital in improving all the factors measured (P≤0.04), except that the difference for relief of spasm was borderline (P=0.10) at the end of day 2.

Overall Improvement. Final evaluation of overall response to therapy in each of the three groups (Table 6) showed carisoprodol to be statistically significantly more effective than both placebo and butabarbital (P<0.01):

Side Effects. One patient receiving butabarbital had drowsiness and dropped out of the study after taking six tablets. No other adverse experiences were noted for any of the patients in this study.

Discussion

An unexpected finding, upon analysis of the data, was that, despite careful randomization, the baseline symptom severity scores for the carisoprodol group were significantly higher for several factors than were the baseline scores of either of the other two treatment groups. Apparently the sample size was simply not large enough to produce comparability of all factors in each of the groups.

The question of what influence this disparity may have had on the outcome is provocative, but probably not completely answerable. On the one hand, the scoring system favored a possibility for greater improvement in the group with greater initial symptom severity, since improvement was calculated by subtracting scores at each evaluation period from baseline scores. On the other hand, it is common clinical experience that severe pain is harder to relieve, and requires more potent medication, than mild pain. Thus the better performance of carisoprodol in this more severely ill group would tend to strengthen the meaning of the results. My own judgment is that, even though the method of scoring and analysis favored the more severely ill carisoprodol group, the magnitude of the difference in results between it and the other two groups was such as to represent a genuine superiority of this treatment over the others. This conclusion is supported by the fact that the critical symptom

TABLE 6.—*Comparison of Ratings, all Factors Combined*

Overall Response	*Carisoprodol*	*Butabarbital*	*Placebo*
Excellent	7	0	0
Good	5	2	2
Fair	0	6	1
Poor	1	6	5
Worse	1	1	6
Total No. of Patients	14	15	14

Carisoprodol significantly better than butabarbital ($P < 0.01$)
Carisoprodol significantly better than placebo ($P < 0.01$)

"spasm" showed significantly greater improvement with carisoprodol than with either butabarbital or placebo, despite the fact that the initial severity scores for this symptom were closely comparable in the three groups.

Conclusions

Since carisoprodol was shown to be significantly more effective than placebo in relieving the symptoms of the "low back syndrome," it can be concluded that it is an active medication, useful for the relief of pain and spasm in acute traumatic musculoskeletal conditions such as those treated. Since carisoprodol was found to be significantly better in all factors measured than butabarbital in the dosage used, it can be concluded that its effectiveness is not due solely to a sedative action, but is also related to its muscle relaxant activity.

TRADE AND GENERAL NAMES OF DRUGS

Soma® ..... carisoprodol

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THE PUS AND THE HISTORY?—TREAT FOR GONORRHEA

I am one of those individuals who feel that the diagnosis of gonorrhea is essentially clinical. Laboratory work helps but I still like to go back to the patient and get a history. I still like to look at the patient and see if he has the disease rather than rely solely on laboratory tests. The male who has a thick, creamy, yellow, purulent discharge, pain on urination, and a history of recent sexual exposure has gonorrhea; and somebody will have to prove to me that he doesn't. The female who has an endocervicitis and a little abdominal pain when you flip her uterus around, particularly if she has a history of promiscuous sexual exposure, also has gonorrhea. Both the female and the male are treated in our clinics on clinical evidence. We obtain smears and cultures and send them to the laboratory. But we make up our minds when we see the patient as to whether we are dealing with possible gonorrhea. We make a clinical diagnosis and institute therapy on the first visit, if at all possible. I believe we have to bend over backward and probably "overdiagnose" and then institute therapy immediately, particularly in the present epidemic situation.

—WALTER H. SMARTT, M.D., Chief, Venereal Disease Control Division, Los Angeles County Health Department, Los Angeles

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